

PATENT COOPERATION TREATY

*M.H.*

**PCT**

**NOTIFICATION OF ELECTION**

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Assistant Commissioner for Patents  
United States Patent and Trademark  
Office  
Box PCT  
Washington, D.C.20231  
ÉTATS-UNIS D'AMÉRIQUE

in its capacity as elected Office

<b>Date of mailing (day/month/year)</b> 22 December 1999 (22.12.99)	
<b>International application No.</b> PCT/US99/10579	<b>Applicant's or agent's file reference</b> PU3491WO
<b>International filing date (day/month/year)</b> 14 May 1999 (14.05.99)	<b>Priority date (day/month/year)</b> 15 May 1998 (15.05.98)
<b>Applicant</b> LENHARD, James, Martin et al	

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:  
17 November 1999 (17.11.99)

☐ in a notice effecting later election filed with the International Bureau on:  
\_\_\_\_\_

2. The election ☒ was  
☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

<p>The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland</p> <p>Facsimile No.: (41-22) 740.14.35</p>	<p>Authorized officer Kiwa Mpay</p> <p>Telephone No.: (41-22) 338.83.38</p>
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# PATENT COOPERATION TREATY

## PCT

### INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference <b>PU3491WO</b>	<b>FOR FURTHER ACTION</b> See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. <b>PCT/US99/10579</b>	International filing date ( <i>day/month/year</i> ) <b>14 MAY 1999</b>	Priority date ( <i>day/month/year</i> ) <b>15 MAY 1998</b>
International Patent Classification (IPC) or national classification and IPC Please See Supplemental Sheet.		
Applicant <b>GLAXO GROUP LIMITED</b>		

<p>1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of <u>5</u> sheets.</p> <p><input type="checkbox"/> This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority. (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p>These annexes consist of a total of <u>0</u> sheets.</p>
<p>3. This report contains indications relating to the following items:</p> <ul style="list-style-type: none"> <li>I <input checked="" type="checkbox"/> Basis of the report</li> <li>II <input type="checkbox"/> Priority</li> <li>III <input type="checkbox"/> Non-establishment of report with regard to novelty, inventive step or industrial applicability</li> <li>IV <input type="checkbox"/> Lack of unity of invention</li> <li>V <input checked="" type="checkbox"/> Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</li> <li>VI <input type="checkbox"/> Certain documents cited</li> <li>VII <input type="checkbox"/> Certain defects in the international application</li> <li>VIII <input type="checkbox"/> Certain observations on the international application</li> </ul>

Date of submission of the demand  <b>17 NOVEMBER 1999</b>	Date of completion of this report  <b>11 JULY 2000</b>
Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231  Facsimile No. (703) 305-3230	Authorized officer  <div style="text-align: center;">   <b>JA-NA HINES</b> </div> Telephone No. (703) 308-0196

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US99/10579

**I. Basis of the report**

1. This report has been drawn on the basis of *(Substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments)*:

☒ the international application as originally filed.

☒ the description, pages (See Attached) , as originally filed.

pages \_\_\_\_\_ , filed with the demand.

pages \_\_\_\_\_ , filed with the letter of \_\_\_\_\_.

pages \_\_\_\_\_ , filed with the letter of \_\_\_\_\_.

☒ the claims, Nos. (See Attached) , as originally filed.

Nos. \_\_\_\_\_ , as amended under Article 19.

Nos. \_\_\_\_\_ , filed with the demand.

Nos. \_\_\_\_\_ , filed with the letter of \_\_\_\_\_.

Nos. \_\_\_\_\_ , filed with the letter of \_\_\_\_\_.

☒ the drawings, sheets/fig (See Attached) , as originally filed.

sheets/fig \_\_\_\_\_ , filed with the demand.

sheets/fig \_\_\_\_\_ , filed with the letter of \_\_\_\_\_.

sheets/fig \_\_\_\_\_ , filed with the letter of \_\_\_\_\_.

2. The amendments have resulted in the cancellation of:

☒ the description, pages None .

☒ the claims, Nos. None .

☒ the drawings, sheets/fig None .

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the ~~Supplemental Box~~ Additional observations below (Rule 70.2(c)).

4. Additional observations, if necessary:

NONE

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US99/10579

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement****1. STATEMENT**

Novelty (N)	Claims (Please See supplemental sheet)	YES
	Claims (Please See supplemental sheet)	NO
Inventive Step (IS)	Claims (Please See supplemental sheet)	YES
	Claims (Please See supplemental sheet)	NO
Industrial Applicability (IA)	Claims (Please See supplemental sheet)	YES
	Claims (Please See supplemental sheet)	NO

**2. CITATIONS AND EXPLANATIONS**

1. Claims 1-18, 20, 23-28, 30-32, 34, 37-43, 45-47, 49, 52-58, 60, 63, 65-67 and 69-71 lack novelty under PCT Article 33(2) as being anticipated by Paulik et al. (Pharm. Res). Paulik et al., teaches the development of infrared imaging to measure thermogenesis in cell culture and thermogenic effects of uncoupling protein-2, troglitazone and Beta-adrenoceptor agonists. the authors developed a robust non-invasive technique to measure real time thermogenesis of cells cultured in microtiter plates using infrared thermography. By showing heat production in yeast increased after transforming the cells with mitochondrial uncoupling protein 2 (UCP2) or treating the cells with a mitochondrial uncoupler carbonyl cyanide p-(trifluoromethoxy)phenylhydrazone (FCCP). Also, the method shows a selective beta-adrenoceptor agonist, stimulated an acute thermogenic response in adipocytes and this process was not blocked by the protein synthesis inhibitor, cycloheximide. The data showed increased UCP synthesis resulted in increased thermogenesis in yeast. These results, taken with the high resolution and robustness of the this approach indicate infrared imaging can be adapted to a variety of thermogenic studies using cultured cells. figure 1 teaches an apparatus which can measure and provide infrared images. Figures 2-5 teach the results achieved after contacting the sample with the test agent and measuring and comparing the results.

Therefore, Paulik et al., teaches the invention of the instant application.

2. Claims 19, 33 and 48 lack an inventive step under PCT Article 33(3) as being obvious over Paulik et al. (pharm. res.) in view of Adachi et al. (US Patent 5,445,157). Paulik et al., has been discussed above, however it does not teach using tumor cells in this method. Adachi et al., teaches a thermographic endoscope which is capable of detecting a temperature distribution in a part under inspection and finding abnormal cells even if the temperature difference between the normal and abnormal cell is small. Thermographic endoscope includes an infrared image forming devices. Abnormal cells evaluated includes cancer cells. The device can also be inserted into a (Continued on Supplemental Sheet.)

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US99/10579

**Supplemental Box**

(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: Boxes I - VIII

Sheet 10

**CLASSIFICATION:**

The International Patent Classification (IPC) and/or the National classification are as listed below:

IPC(7): H01L 29/04; G01N 7/00, 25/18, 25/08, 27/416, 1/18, 21/62 and US Cl.: 257/59, 72; 436/147, 149, 150, 151, 155, 157, 171

**I. BASIS OF REPORT:**

This report has been drawn on the basis of the description,  
pages, 1-50, and sequence listing pages 1-2, as originally filed.  
pages, NONE, filed with the demand.  
and additional amendments:  
NONE

This report has been drawn on the basis of the claims,  
numbers, 1-71, as originally filed.  
numbers, NONE, as amended under Article 19.  
numbers, NONE, filed with the demand.  
and additional amendments:  
NONE

This report has been drawn on the basis of the drawings,  
sheets, 1-27, as originally filed.  
sheets, NONE, filed with the demand.  
and additional amendments:  
NONE

**V. 1. REASONED STATEMENTS:**

The report as to Novelty was positive (YES) with respect to claims 19, 21-22, 29, 33, 35-36, 44, 48, 50-51, 59, 61-62, 64 and 68.

The report as to Novelty was negative (NO) with respect to claims 1-18, 20, 23-28, 30-32, 34, 37-43, 45-47, 49, 52-58, 60, 63, 65-67, 69-71.

The report as to Inventive Step was positive (YES) with respect to claims 29, 44, 59, 61-62, 64, 68.

The report as to Inventive Step was negative (NO) with respect to claims 1-28, 30-43, 45-58, 60, 63, 65-67, 69-71.

The report as to Industrial Applicability was positive (YES) with respect to claims 1-71.

The report as to Industrial Applicability was negative (NO) with respect to claims None.

**V. 2. REASONED STATEMENTS - CITATIONS AND EXPLANATIONS (Continued):**

body cavity.

Therefore it would have been obvious to analysis cancer cells as taught by Adachi et al., in the method of Paulik et al., because Adachi et al., teaches that it is well known in the art to monitor, measure and compare temperature differences between abnormal cancer cells and normal ones.

3. Claims 21-22, 35-36 and 50-51 lack an inventive step under PCT Article 33(3) as being obvious over Paulik et al., (Pharm Res.) in view of SHARP KABUSHIKI KAISHA, (GB 2,266,182). Paulik et al., has been discussed above, however it does not teach the use of plant or fungal cells. Watsuji et al., teaches data acquisition, processing devices and biosensors for use in the information technology field. Biological macromolecules such as proteins, enzymes, glycoproteins, nucleic acids and products of recombinant technology can be analyzed.

Therefore, it would have been obvious to one of ordinary skill in the art to analyze plant or fungal cells as taught by Watsuji et al., in the method of Paulik et al., because watsuji et al., teaches a variety of cell types can be analyzed.

Claims 29, 44, 59, 61-62, 64 and 68 meet the criteria set out in PCT Article 33(2)-(3) because the prior art does not teach or fairly suggest the claimed invention.

Claims 1-71 meet the criteria set out in PCT Article 33(4) for industrial applicability.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US99/10579

**Supplemental Box**

(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: Boxes I - VIII

Sheet 11

\_\_\_\_\_ NEW CITATIONS \_\_\_\_\_

NONE

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**PCT**

WORLD INTELLECTUAL PROPERTY ORGANIZATION  
International Bureau



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification <sup>6</sup> : <b>H01L 29/04, G01N 7/00, 25/18, 25/08, 27/416, 1/18, 21/62</b>		<b>A1</b>	(11) International Publication Number: <b>WO 99/60630</b>
			(43) International Publication Date: 25 November 1999 (25.11.99)
(21) International Application Number: PCT/US99/10579 (22) International Filing Date: 14 May 1999 (14.05.99) (30) Priority Data: 60/085,736                      15 May 1998 (15.05.98)                      US (63) Related by Continuation (CON) or Continuation-in-Part (CIP) to Earlier Application US    60/085,736 (CIP) Filed on                                      15 May 1998 (15.05.98) (71) Applicant (for all designated States except US): GLAXO GROUP LIMITED [GB/GB]; Glaxo Wellcome House, Berkeley Avenue, Greenford, Middlesex UB6 0NN (GB). (72) Inventors; and (75) Inventors/Applicants (for US only): LENHARD, James, Martin [US/US]; Glaxo Wellcome Inc., Five Moore Drive, P.O. Box 13398, Research Triangle Park, NC 27709 (US). PAULIK, Mark, Andrew [US/US]; Glaxo Wellcome Inc., Five Moore Drive, P.O. Box 13398, Research Triangle Park, NC 27709 (US).		(74) Agents: LEVY, David, J.; Glaxo Wellcome Inc., Five Moore Drive, P.O. Box 13398, Research Triangle Park, NC 27709-3398 (US) et al. (81) Designated States: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG). <b>Published</b> <i>With international search report.</i> <i>Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i>	
(54) Title: INFRARED THERMOGRAPHY			
(57) Abstract			
<p>The present invention relates, in general, to thermography and, in particular, to a method of using infrared thermography to monitor physiological and molecular events that elicit a thermogenic response in animals (including humans), plants, tissues, cells and cell-free systems. The present method can be used for screening, identifying, and ranking drug candidates for multiple diseases, disorders and conditions.</p>			

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DE	Germany	LK	Sri Lanka	SE	Sweden		
DK	Denmark	LR	Liberia	SG	Singapore		
EE	Estonia						



## INTERNATIONAL SEARCH REPORT

International application No.

PCT/US99/10579

## A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) : H01L 29/04; G01N 7/00, 25/18, 25/08, 27/416, 1/18, 21/62

US CL : 257/59, 72; 436/147, 149, 150, 151, 155, 157, 171

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : NONE

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched  
ADONISElectronic data base consulted during the international search (name of data base and, where practicable, search terms used)  
CAPLUS, APS, BIOSIS, WPIDS, STN

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	PAULIK, M.A. et al. Development of Infrared Imaging to Measure Thermogenesis in Cell Culture. FASEB Journal. April 1998, Vol. 12, No. 8, page A1302, #D5, entire document.	1-12, 14-18, 20, 25-26, 28, 30-32, 34, 39, 41-43, 45-47, 49, 54-56, 60-63, 65-67, 69-71
X	PAULIK, M.A. et al. Development of Infrared Imaging to Measure Thermogenesis in Cell Culture: Thermogenic Effects of Uncoupling Protein-2, Troglitazone, and Beth-Adrenoceptor Agonists. Pharm. Res. March 1998, Vol. 15, No. 6, pages 944-949, see entire document.	1-18, 20, 23-28, 30-32, 34, 37-43, 45-47, 49, 52-58, 60, 63, 65-67, 69-71

☒ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:	*T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
*A* document defining the general state of the art which is not considered to be of particular relevance	*X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
*E* earlier document published on or after the international filing date	*Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
*L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	*G* document referring to an oral disclosure, use, exhibition or other means
*G* document referring to an oral disclosure, use, exhibition or other means	*P* document published prior to the international filing date but later than the priority date claimed
*P* document published prior to the international filing date but later than the priority date claimed	*F* document member of the same patent family

Date of the actual completion of the international search  
31 AUGUST 1999

Date of mailing of the international search report

17 SEP 1999

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## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US99/10579

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 5,445,157 A (ADACHI et al.) 29 August 1995, col 2-3.	1-10, 19, 33, 48
Y	GB 2 266 182 A (SHARP KABUSHIKI KAISHA) 20 October 1993, pages 2-11.	21-22, 35-36, 50-51